

CELL CULTURE MEDIUM FOR EUKARYOTIC CELLS

FIELD

[0001] The present invention generally pertains to a cell culture medium for eukaryotic cells and the production of natural and recombinant products derived therefrom.

BACKGROUND

[0002] Cell culture manufacturing technology is widely used for the production of biopharmaceuticals. As the demand for biopharmaceuticals increase, demand for increase in cell growth, viability and protein production have also increased considerably. Much effort is now being placed on methods and strategies for growing, feeding, and maintaining cell cultures.

[0003] New cell culture methods that provide even incremental improvements in recombinant protein production are valuable, given the challenges and expense of large scale cell culture processes and the growing demand for greater quantities of and lower costs for biological products. Improvements to cell culture processes, recombinant polypeptide expression, titer, and cell viability that can lead to higher production levels, thereby reducing the costs associated with manufacturing protein therapeutics are needed.

SUMMARY

[0004] Growth in the development, manufacture and sale of protein-based biopharmaceutical products has led to an increasing demand for production methods that can improve production of the biopharmaceutical products.

[0005] Embodiments disclosed herein address the aforementioned demands by providing methods and media for manufacture of such biopharmaceutical products.

[0006] The disclosure, at least in part, provides a cell culture medium for eukaryotic cells.

[0007] In one exemplary embodiment, the cell culture medium for eukaryotic cells can comprise a basal medium. In one aspect of this embodiment, the cell culture medium can further comprise 5-methylthioadenosine. In another aspect of this embodiment, the cell culture medium can comprise at least about 10 nM of 5-methylthioadenosine. In yet another aspect of this embodiment, the cell culture medium can comprise about 10 nM to about 200 nM of 5-methylthioadenosine. In one aspect of this embodiment, the cell culture medium can further comprise nicotinamide. In another aspect of this embodiment, the cell culture medium can comprise at least about 50 nM of nicotinamide. In yet another aspect of this embodiment, the cell culture medium can comprise about 2000 nM of 5-nicotinamide. In one aspect of this embodiment, a titer of a protein grown in the cell culture medium is at least about 2% greater than another cell culture medium not comprising at least about 10 nM 5-methylthioadenosine. In another aspect of this embodiment, a titer of a protein grown in the cell culture medium is at least about 2% greater than another cell culture medium not comprising at least about 50 nM nicotinamide. In one aspect of this embodiment, the cell culture medium can optionally further comprise one or more acids selected from lactic acid, phenyl lactic acid, indolelactic acid, succinic acid, alpha-hydroxyisovaleric acid, alpha-hydroxyisocaproic acid, 2-(4-hydroxy-phenyl)lactic acid, or 2-hydroxy-3-methylvaleric acid, salts of these acids, esters of these

acids and combinations thereof. In one aspect of this embodiment, the cell culture medium can optionally further comprise sugars, amino acids, vitamins, salts, trace metal ions, purines, and/or pyrimidines. In one aspect of this embodiment, the cell culture medium can comprise salts or esters of 5-methylthioadenosine. In another aspect of this embodiment, the cell culture medium can comprise salts or esters of nicotinamide. In one aspect of this embodiment, the cell culture medium can have a pH of about 6.5 to about 8. In one aspect of this embodiment, the cell culture medium does not have a protein derived from an animal. In one aspect of this embodiment, the cell culture medium can be a serum-free medium. In one aspect of this embodiment, the cell culture medium can be a chemically-defined medium.

[0008] In one exemplary embodiment, the cell culture medium for eukaryotic cells can comprise a feed medium. In one aspect of this embodiment, the cell culture medium can further comprise 5-methylthioadenosine. In another aspect of this embodiment, the cell culture medium can comprise at least about 10 nM of 5-methylthioadenosine. In yet another aspect of this embodiment, the cell culture medium can comprise about 10 nM to about 200 nM of 5-methylthioadenosine. In one aspect of this embodiment, the cell culture medium can further comprise nicotinamide. In another aspect of this embodiment, the cell culture medium can comprise at least about 50 nM of nicotinamide. In yet another aspect of this embodiment, the cell culture medium can comprise about 50 nM to about 2000 nM of 5-nicotinamide. In an alternate aspect of this embodiment, the cell culture medium can further comprise 5-methylthioadenosine and nicotinamide. In one aspect of this embodiment, the cell culture medium can optionally further comprise one or more acids selected from lactic acid, phenyl lactic acid, indolelactic acid, succinic acid, alpha-hydroxyisovaleric acid, alpha-hydroxyisocaproic acid, 2-(4-hydroxy-phenyl)lactic acid, or 2-hydroxy-3-methylvaleric acid, salts of these acids, esters of these acids and combinations thereof. In one aspect of this embodiment, the cell culture medium can optionally further comprise sugars, amino acids, vitamins, salts, trace metal ions, purines, and/or pyrimidines. In one aspect of this embodiment, the cell culture medium can comprise salts or esters of 5-methylthioadenosine. In another aspect of this embodiment, the cell culture medium can comprise salts or esters of nicotinamide. In one aspect of this embodiment, the cell culture medium can have a pH of about 6.5 to about 8. In one aspect of this embodiment, the cell culture medium does not have a protein derived from an animal. In one aspect of this embodiment, the cell culture medium can be a serum-free medium. In one aspect of this embodiment, the cell culture medium can be a chemically-defined medium. In one aspect of this embodiment, the cell culture medium can optionally comprise nicotinamide. In one aspect of this embodiment, a titer of a protein grown in the cell culture medium is at least about 2% greater than another cell culture medium not comprising at least about 10 nM 5-methylthioadenosine. In another aspect of this embodiment, a titer of a protein grown in the cell culture medium is at least about 2% greater than another cell culture medium not comprising at least about 50 nM nicotinamide.

[0009] The disclosure, at least in part, provides a method of producing a protein.

[0010] In one exemplary embodiment, the method of producing a protein can comprise culturing eukaryotic cells having a nucleic acid encoding the protein in a cell culture